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Piezoelectric Materials for Medical Applications

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Abstract

This chapter describes the history and development strategy of piezoelectric materials for medical applications. It covers the piezoelectric properties of materials found inside the human body including blood vessels, skin, and bones as well as how the piezoelectricity innate in those materials aids in disease treatment. It also covers piezoelectric materials and their use in medical implants by explaining how piezoelectric materials can be used as sensors and can emulate natural materials. Finally, the possibility of using piezoelectric materials to design medical equipment and how current models can be improved by further research is explored. This review is intended to provide greater understanding of how important piezoelectricity is to the medical industry by describing the challenges and opportunities regarding its future development.

Keywords: piezoelectric materials, biotechnology, biomedical applications and devices, vital signs, sensors, cell regeneration

1. Introduction

Piezoelectricity is a quality of material asymmetry that leads to the conversion of electric signals into physical deformation and conversely physical deformation into electric signal. An applied pressure causes movement of the dipole moment within the material, and a flow of charges if crystals are aligned [1]. This makes piezoelectricity useful for a variety of industry purposes, particularly those related to vibrational generation and actuation. Commercialized applications for piezoelectricity include timekeeping using quartz resonance, microphones, radio antenna oscillators, speakers, hydrophones, and fuel injection [2, 3]. More experimental technology includes energy harvesting and electronic sensing [2]. The most commonly used ceramic piezoelectric material is lead zirconium titanate (PZT), because its physical properties

can be tailored by composition, it has a high piezoelectric coefficient, and it is cheap to manufacture [4]. The most common piezoelectric polymer, used for its large strain value, is polyvinylidene fluoride (PVDF) and its copolymers, such as P(VDF-TrFE) [5–8]. A wide variety of composites and nanostructure materials have also been developed and can be fabricated as thin films, discs, or stacked sheets [2, 3, 9–13].

In the case of biomedical engineering, many conventional means of using piezoelectric devices are not applicable because of the structure of biological systems. Issues such as size limitations, biological compatibility, and flexibility have led to investigation into polymer, composite, nanostructured, and lead-free piezoelectric materials. One way to develop biomedical devices is to look at the piezoelectric structures inside the body and how they can be emulated to develop piezoelectric medical technology. In the first section of this book, we discuss piezo-electric materials present in the body. Then we describe how piezoelectric materials can be used for diagnosing illnesses and providing medical treatment. Our purpose is to inform the readers of challenges and different approaches applicable to developing a wide variety of medical technology.

2. Biological piezoelectric materials

There are many reviews which cover subsections of biological piezoelectric materials; these reviews explain topics such as piezoelectricity in bone [14] or biopolymers [15]. However, we seek to present a broader overview of the topic and how it can be used to develop technology. Much of the original work on discovering piezoelectricity in the body was done by Eiichi Fukada [15–18]. His work showed the presence of piezoelectricity in bone, aorta, muscles, tendons, and intestines [15–18]. Since that time, many further studies have contributed to the overall knowledge of the body's piezoelectric characteristics, their origins, and how they can be applied in medical science.

The organic piezoelectric effects in the human body are attributed to the lack of symmetry in most biological molecules, which may make piezoelectricity a fundamental biological property [19]. In particular, proteins seem to drive the piezoelectric qualities of most organs. The basic building blocks of proteins within the human body are amino acids. These make up molecules such as collagen, keratin, and elastin which are highly prevalent in the organs examined by Fukada and other researchers [15–18]. Amino acids in pure form have their own piezoelectric properties due to the presence of dipoles derived from the polar side groups seen in **Figure 1**. It is the reorientation and change in dipole moments in biological macromolecules under stress that gives them piezoelectric properties [20, 21]. At least 15 amino acids, mostly the "L" form, exhibit piezoelectric properties; however, γ-glycine and DL-alanine are the strongest amino acid piezoelectrics [22]. Most racemic, or DL mixtures of amino acids do not show piezoelectric properties because their crystal forms are centrosym-metric [23].
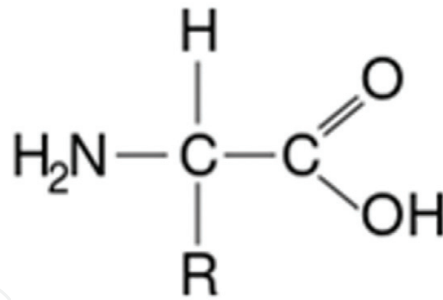
Figure 1. The general structure of amino acids. Reprinted and altered from Ref. [24].

Other biological piezoelectric materials include polymeric L-lactic acid, DNA, and the M13 bacteriophage [25–27]. Like amino acids, the piezoelectric properties of lactic acid come from the carbon–oxygen double bond [25]. DNA's piezoelectric properties originate from internal rotation of the dipoles created by phosphate groups; however, they were primarily observed at lower water content, which makes the bonds holding the DNA helix together weaker [27]. This demonstrates the importance of bonding, structure, and experimental conditions when determining piezoelectric properties. The M13 bacteriophage's piezoelectric effect is caused by extruding proteins and it can be fabricated into thin films that exhibit strengths of 7.8 pm/V [26].

Like the bacteriophage, many organs contain macromolecules which give them piezoelectric properties. Organs with piezoelectric properties can be viewed as amorphous organic material containing structured fibers which give them their piezoelectric properties [19, 28]. Often these fibrils will grow in a helix shape, preventing them from having centrosymmetric symmetry [29]. The overall strength of the piezoelectric effect will depend on the ordering, quantity or composition of these fibers. Bones and tendons have hexagonal symmetry and contain the following piezoelectric constant d_{ij} in the form of Eq. (1) [30]. In this tensor, the "i" subscript represents direction of electric field displacement and the "j" subscript represents the mechanical deformation associated with it [31].

$$d_{ij} = \begin{pmatrix} 0 & 0 & 0 & d_{14} & d_{15} & 0 \\ 0 & 0 & 0 & d_{15} & -d_{14} & 0 \\ d_{31} & d_{32} & d_{33} & 0 & 0 & 0 \end{pmatrix} \tag{1}$$

Molecular structure within the organ changes the organ's overall piezoelectric nature. For example, examination of the epidermis, horny layer, and dermis of the skin revealed that each layer had its own piezoelectric coefficient, the highest being the horny layer. The dermis had a less ordered collagen layer; the horny layer had parallel keratin filaments, and the epidermis α helical keratin tonofibrils [28]. The structure of the keratin horny layer simplified its ability to produce piezoelectric tensors, giving them the form of Eq. (2). The values of piezoelectric coefficients varied based on temperature; however, the highest were seen in the horny layer, on the order of 0.1–0.2 pC/N. The lack of consistency in these measurements is due to the variety in how the molecules were ordered in each sample [28].

$$d_{ij} = \begin{pmatrix} 0 & 0 & 0 & d_{14} & 0 & 0 \\ 0 & 0 & 0 & 0 & -d_{14} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} \qquad (2)$$

Similarly, piezoresponse force measurements (PFM) studies of collagen proved that collagen is the main source of piezoelectricity in the bone and reveal different ordering of collagen fibers results in different piezoresponses, as seen in **Figure 2** [32]. In collagen, there are alternating sections of overlap and gap regions. The collagen fibers are arranged in a staggered way that result in the gap region having one less microfiber. In addition, the molecules in the gap region have less uniform symmetry, and therefore that region does not have as high of a piezo-response [32]. These two studies indicate the piezoelectric response is not merely dependent on the molecular structure, but the structure of the entire organ. **Table 1** gives a description of organs with tested piezoelectric properties and their attributed molecule.

Despite many measurements, it is sometimes difficult for the scientific community to come to a consensus on the exact nature and relevance of *in situ* piezoelectric characteristics. For example, in the case of bone, two groups found contradicting results on the dependency of piezo-electricity in terms of hydration [14, 37]. Some studies on the aorta indicate that it has piezoelectric properties, though results were varied. Two studies, taken over forty years apart showed different orders of magnitude for the studied properties [17, 38]. A lab attempting to verify either of these studies found that there was no piezoelectric response from the aorta [39].
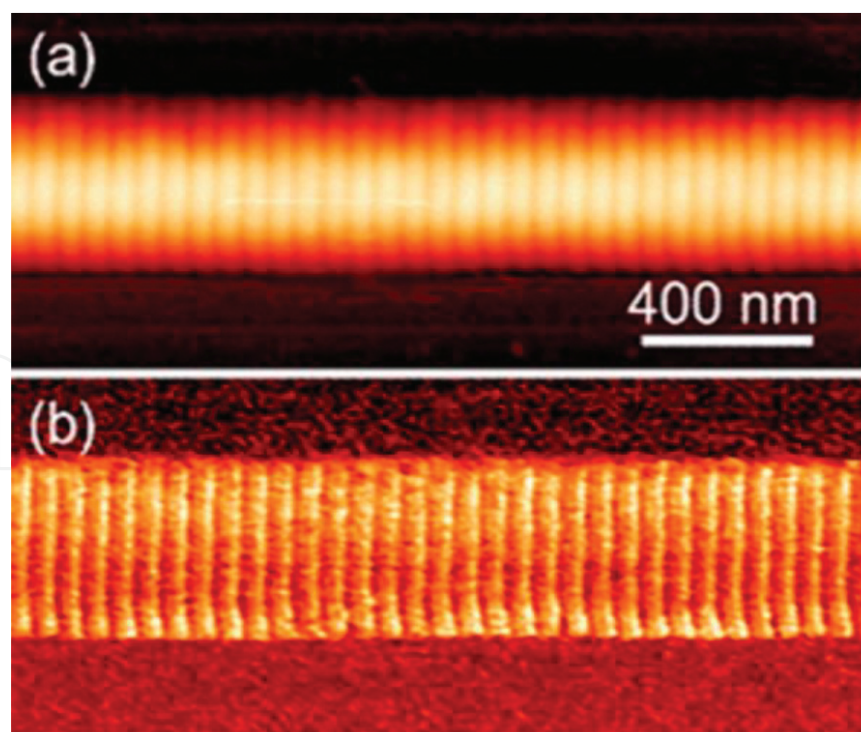

Figure 2. The images show (a) the topology of the collagen and (b) the piezoresponse force microscopy (PFM) image where the collagen can be distinguished from the surrounding tissues and how the gap and overlap regions differ in piezoelectric response. Reprinted from Minary-Jolandan and Yu [32] with permission from ACS Publications.

Organ	Piezoelectric molecule
Muscle	Actin and myosin [18]
Hair	Keratin [16]
Bone	Collagen [32]
Tendon	Collagen [33]
Lung tissue	Elastin [34]
Skin (dermis)	Collagen [28]
Skin (horny layer and epidermis)	Keratin [28]
Breast tissue	Collagen [35]
Outer hair cell	Prestin [36]

Table 1. Tissues with piezoelectric properties and driving source of piezoelectricity.

Historically, piezoelectric potentials were thought to explain Wolff's Law, the fact that bone is strong in areas that are subject to greater amounts of stress [40]. However, later research proved streaming potentials, fluid and ions driven by mechanical loading, may have a greater impact in determining bone properties [41]. However, Ahn *et al.* suggest that piezoelectricity could generate charges that affect the screening potential and the two work in conjunction to promote bone development, a concept which requires experimental testing to verify [40]. Furthermore, the generation of electric fields has been shown to increase bone healing during fracture [42, 43].

Despite the variety of results concerning piezoelectric qualities of the body, they do help in understanding the body's mechanics and how we can develop solutions for human problems. Even if the exact purpose for piezoelectric properties in the body is not known, they still can be used for developing biomedical solutions on both microscopic and macroscopic levels. For example, knowing that amino acids and macromolecules composed of them have piezoelectric properties has inspired the use of biomaterials for human sensors [44]. Using peptides to build piezoelectric sensors eliminates the need for developing other biocompatible materials. For example, the knowledge of previously mentioned virus, M13, led to the alignment of its phages into nanopillars for enhanced piezoelectric properties [45]. The outer hair cell is another structure that piezoelectric properties can be attributed to. Disruption of the cell's electrical potential alters its length; conversely, compression of the cell alters its membrane potential [46]. The motions of the outer hair cell alter how the organ of Corti vibrates, and changes how the inner hairs receive stimulation [36]. Recently, the development of a piezoelectric cochlear implant to mimic the conversion of sound vibration into an electrical signal has been undertaken and will be covered in a later section of this review [47]. Biological structures can serve as examples for the development of piezoelectric structures and biocompatible piezoelectric materials.

In addition, the knowledge of piezoelectric properties can help in disease detection or injury analysis. With the knowledge that piezoelectric tissue properties are determined by proteins, diseases that affect the amount or distribution of these proteins can be detected by piezoelectric sensors. One group proposed that the electromechanical coupling factor, controlled by collagen, could aid in detecting breast cancer [35]. A similar idea was presented for the

detection of atherosclerosis in the aorta, however as mentioned in a prior paragraph the validity of the aorta's piezoelectric nature is still under debate [48]. In this paper, they claimed the PFM amplitude increased as a function of advancing atherosclerosis and could help with early detection of the disease.

Finally, once the effect of piezoelectricity on the body have been studied, piezoelectric materials can be used to promote disease healing. Though the exact reason for piezoelectric qualities have not been fully discovered, studies into bone related injuries have revealed that induced electrical fields can accelerate bone repair and promote the growth of neurons [49, 50]. Because of this, increasing the piezoelectric properties of a synthetic bone material has potential to increase the speed of osteoconduction and subsequently bone repair [51]. Lead free ceramics can be used in conjunction with synthetic bone; however, these materials have problems with ion diffusion which can be controlled by embedding in a ceramic or polymer matrix [50]. In terms of regenerating damaged bone or cartilage, a piezoelectric scaffold may provide the necessary stimulation for cell regrowth, and diminish the need for other growth factors [43]. Typically, scaffolds are made out of polymers, such as PVDF, and can also promote the growth of neurons and wound healing [50].

3. Piezoelectric medical devices

Many biomedical piezoelectric applications exceed the aforementioned purposes of mimicking or employing biological piezoelectric phenomena. In some cases, the choice of material depends mostly on the strength of the piezoelectric effect and the cost of the material. PZT (lead zirconium titanate) and quartz are common piezoelectric materials used in industry. PZT is cheaper, has higher piezoelectric coupling coefficients, and can be manipulated by changing the composition. Quartz, however, is more stable and has consistent properties over a broader temperature range [4]. Developing implants or technology involving direct human contact has more constraints. Ceramics, like quartz, barium titanate, and potassium sodium niobate, are more biocompatible because they do not contain lead [50]. In addition, many biomedical devices require higher flexibility than ceramics can provide, due to the dynamic nature of human motion. Biocompatible polymers include most biological materials and PVDF copolymers. So far, polymer applications of PVDF have included, but are not limited to, biomechanical energy harvesting systems, sensors, and wound scaffolds [50, 52]. The piezoelectric coefficient of the beta phase of PVDF is listed in Eq. (3) [53].

$$d_{ij} = \begin{pmatrix} 0 & 0 & 0 & 0 & d_{15} & 0 \\ 0 & 0 & 0 & d_{24} & 0 & 0 \\ d_{31} & d_{32} & d_{33} & 0 & 0 & 0 \end{pmatrix} \tag{3}$$

3.1. Piezoelectric sensors

Piezoelectric materials can be employed in monitoring many bodily signals because they convert mechanical energy into an electrical signal. They are especially applicable to monitoring dynamic pressure changes; many human vital signs consist of rhythmic activities like the heartbeat or

breathing. Lower pressure systems from (1 Pa-10 kPa) include sound waves and tactile sensing. In the higher end of that range are intraocular pressure and cranial pressure. Higher-pressure systems (10 kPa–100 kPa) correspond to blood pressure measurements and some bodily movements. Piezoelectric sensors can be tailored by structure or material to match the pressure range of the desired quality [54]. Implanted or wearable medical sensors have greater applicability, as the Internet of Things becomes more fully developed. A medical professional or computer algorithm can monitor a patient for early warning signs that may have been missed between scheduled check-ups through their implanted device [55]. **Table 2** lists some literature studies of piezoelectric sensors and their tested applications.

The variety of applications for piezoelectric sensors in the biomedical industry is promising, however much of this technology is still in the research and development phase. Before reaching the market, these devices need to have scalable manufacturing and guaranteed quality for every device [52].

3.1.1. Developing synthetic skin

A specific application for piezoelectric pressure sensing is synthetic skin. As a bare minimum, synthetic skin should provide the magnitude of contact force and approximate location of

Material	Applications	Device characteristics	Refs.
Prawn cell	Wrist pulse	100 Hz−10 MHz range	[56]
PVDF	Human voice detection Hand motion Breathing rate	50–1000 Hz range	[57]
$(Na_{0.5},K_{0.5})NbO_3$ (NKN) thin film	Cardio mechanical electric sensor	10 Hz resonance	[58]
PVDF	Wrist pulse Measuring peripheral arterial pressure pulse		[59]
AlN	Heart and respiration patterns for sleep apnea	Tested over 0.1–10 Hz	[60]
PVDF	Heartbeat and respiration detection	Tested 0.1–2 Hz	[61]
Fish gelatin	Joint movement Human vocal cord movement Radial artery pulses	d_{33}–20 pm/V Stability over 108,000 cycles	[62]
PZT	Eye fatigue via eyelid motion		[63]
Poly-L-lactic acid	Lung pressure Eye pressure Brain pressure	Biodegradable Stability over 108,000 cycles	[64]
Piezoelectric ceramic	Vision correction	Force sensitivity 0.1×10^{-2} N to 5×10^{-2} N 0.01–5 Hz	[65]
PVDF	Food detection by swallowing pattern	Limit of detection: 1 Hz Tested over 1–5 Hz	[66]

Table 2. Examples of piezoelectric sensors and their applications.

contact with the sensitivity of normal skin [53]. For humans, mechanoreceptors have a range from 3 to 400 Hz, and a spatial resolution of 1–2 mm [67]. Ideally, it would also provide information about temperature changes or humidity [68]. Human skin itself acts as a vibrational sensor; it is structured to amplify tactile stimulation [69]. Piezoelectric force transducers offer a solution to quantifying and locating contact forces [53]. The use of polymers for synthetic skin is popular because of their similarity in texture and flexibility to human skin [70]. Polymers can be molded to emulate human characteristics, such as fingerprints to enhance their sensitivity [69]. Processing techniques, such as electrospinning, can increase response by aligning the molecular dipoles [25]. In a similar way, using hybrid materials or structuring ceramics and polymers can yield higher piezoelectric properties [71, 72].

Though there are many materials, which can be used for this purpose, most are structured in arrays. A unit in the array will send an electrical signal describing the characteristic of the force. In prosthetics, the electric signal will arrive at a location which still can perceive tactile senses [53]. One of the problems with arrays is interference between signals, otherwise known as crosstalk. During crosstalk, neighboring units are affected by the unit undergoing force and send their own signal. This can lead to an ill-defined contact region, which can be fixed using the installation of transistors or through triangulation of the signal [53, 68].

3.1.2. Biological quartz microbalance

One other interesting application of piezoelectric sensors is the detection of disease or odor through a change in chemical composition of a sensor. The quartz microbalance is used for a variety of purposes, such as gas detection [73], composition analysis, and chirality classification [74]. It can also sense changes in liquid density or viscosity [75]. This method relies on mass changes in a coating film around the crystal. Quartz microbalances generally operate in a 5–10 MHz range; the accumulation of mass can be quantified by the Sauerbrey equation (Eq. (4)) [75, 76]. An increase in mass indicates a decrease in the frequency of quartz vibration [76]. When this mass becomes too great (>2%) this relationship becomes inaccurate, and a better approximation is needed [74]. In this type of sensor, biological molecules are imbedded or attached to piezoelectric materials. This technology can also be used for detection of bacteria and biomolecules.

$$\frac{\Delta f}{f_0} = -\frac{\Delta m}{m} \tag{4}$$

The detection of bacteria or biomolecules usually involves the incorporation of a biomolecule in an exterior film. One method of detecting glucose uses the enzyme hexokinase embedded in a polymer matrix. The glucose binds to the enzymes at a rate proportional to its concentration in solution [77]. In another glucose detection system, the frequency of the quartz was increased. The sensor was coated with dextran and Concanavalin A. The dextran preferentially binds to the glucose, therefore the presence of glucose causes the release of Concanavalin A. Glucose has a lower molecular weight, and therefore the frequency increased with its detachment. This method of glucose detection is advantageous because it does not involve the use of enzymes; however has a lower detection range [78]. The quartz microbalance may also be applicable to developing bioelectronic olfactory replacements. It has been used to detect

hazardous odorants such as diacetyl, which can cause damage to the lung if inhaled, and could be used to measure other odors [79]. Unfortunately, some of the quartz microbalance equipment is bulky and requires complicated molecules as indicators. One of the olfactory biosensors is 14 mm in diameter [80]. If the synthetic nose to be used for many compounds, the size may be too large to be practical. In addition, sensors based on biomolecules, such as the glucose have problems with biological stability [78]. These problems need to be fixed before they can be viewed as commercially viable.

3.1.3. Cochlear implants

The destruction of inner ear cells results in severe hearing loss and is most commonly treated by cochlear implants. Though the current technology allows for recovery from deafness, it is incompatible with water and has very high-power requirements [81]. Piezoelectric materials can be used for creating an artificial basilar membrane (ABM). The membrane performs mechanical frequency selectivity for the cochlea. Varying physical rigidity and thickness of the basilar membrane allows it to perform its duty, and likewise piezoelectric materials can filter out frequency based on their physical properties [82]. Ceramics, such as PZT or AlN films, can be fabricated in beam or cantilever arrays with lengths corresponding with different resonance frequencies [81, 83]. Alternatively, devices based on PVDF or P(VDF-TrFE) membranes have been fabricated [47, 83–85]. The typical range of human hearing is 20 Hz–20 kHz. The fabricated PVDF membrane was able to detect signals in the 100 Hz–10 kHz range, which encompasses the range of human vocalizations [84]. Many experimental cochlear ABMs need increased sensitivity, stability, and size reduction to be practically used [83].

3.2. Beyond sensors

3.2.1. Piezoelectric surgery

In addition to creating implants, piezoelectricity can be used in a variety of medical treatments, most of which depend on the vibrational properties of the piezoelectric device. Unlike implanted devices, piezoelectric devices needed for surgery do not need to be biocompatible, because they do not come in contact with human cells. Therefore, many external devices will make use of lead zirconate titanate (PZT), as it is easier to produce [86]. The typical piezosurgical devices will consist of stacked rings which are given an applied voltage. The stacked actuator design increases the actuator efficiency because the electric field is determined by the applied voltage and the thickness (Eq. (5)) [87]. The strain is proportional to the electric field if the thickness of the actuator is decreased, a higher strain can be generated for the same amount of voltage.

$$E = \frac{V}{t} \tag{5}$$

The resulting vibration will be transduced to the tip, which is installed in such a way that it will amplify vibrations, because traditionally ceramics are more brittle and do not display much displacement [88].

In surgery, piezoelectric devices, such as the ultrasonic lancet, are used for delicate operations to preserve surrounding tissue. By controlling the micromovements of the oscillating device, damage to soft tissues can be avoided, and the separation between interfaces is easily accomplished. Alternatives to piezosurgery, such as a chisel and hammer or rotating saw are seen as more invasive, have potential to lacerate non-discriminatorily [89]. Hard tissues, such as mineralized bones are damaged by frequencies of 25–39 kHz, however neurovascular tissue is cut at frequencies higher than 50 kHz. There are no macrovibrations which may cause discomfort to the patient or disturbance of surrounding tissue [90]. The tip oscillates in a linear direction, and can span the distance of 60–200 μm [86].

The first use of piezosurgery was the dental industry, with applications like removal of implants, bone harvesting, and inferior alveolar nerve detachment [91]. Many such surgeries require working in small spaces and do not require larger incisions on the bone material. The removal of implants takes advantage of how the ultrasonic vibrations target the interfacial layer, and weaken the implant's attachment to bone. This reduces the adhesion forces and allows the implant to be removed with fewer incisions. In a similar way, the collection of graft material is another excellent use of an ultrasonic lancet. After making preliminary cuts with a saw, the ultrasonic vibrations reduce the need for chisel strikes [91]. In surgery performed on the lower jawline, protecting the inferior alveolar nerve is important to patient recovery [92]. As said previously, the use of piezosurgery prevents the damage of these nerve tissues. Another benefit in all surgeries is particle breakdown caused by ultrasonic activity, which makes visibility easier [92].

Piezosurgery has some other applications in neurosurgery and orthopedic surgery; however, it is limited in equipment fragility and associated expenses [86, 90]. The tip of the device fractures, creating the need for replacements [88]. It also takes longer to perform operations, and can damage tissue through heating. Irrigation is required to keep the area cool, and larger scale devices are used for macrosized surgeries [86].

3.2.2. Ultrasonic dental scaling

A piezoelectric dental scalar also has piezoelectric ceramic rings (**Figure 3**) on the inside to induce axial vibrations, and operates at ultrasonic frequencies [93]. Ultrasonic dental scalers operate in the range of 25–50 kHz, and oscillate parallel to the tooth surface over a range of 10–100 μm [94]. Its purpose is to remove accumulated biofilms from the tooth surface and for treatment of root canals. The vibrations of the tip break down the calculus (tartar) and plaque which have formed on the tooth's enamel surface. Because of the tip's quick speed, when the irrigation water passes over the scalar, micro- and nanosized bubbles form around its curve and tip [95, 96]. When these
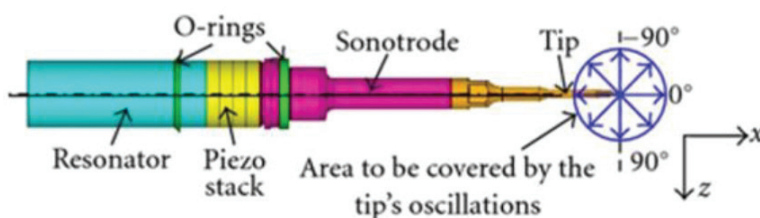

Figure 3. The stacked actuator design and other components of an ultrasonic dental scaler. Reprinted from Engelke et al. [93] with permission from Hindawi.

bubbles collapse, cavitation forces create shock waves cleaning the tooth. This adds to the ultrasonic scalar's effectiveness, and further investigation of the cavitation's effects could lead to new dental technology which further reduces scaler contact with teeth [97].

The oscillation pattern of the scaler depends on the type of tip chosen [93] and the effectiveness of the scaler varies depending on how it is used. Influencing factors can be the lateral force, tip angle, and power setting [98]. Increasing the power on the ultrasonic scalar too much will scratch a tooth's protective enamel surface, increasing the tooth's surface roughness and causing damage to the surrounding tissues. The variety of ultrasonic scalers' operating conditions demonstrates the need for research on appropriate forces needed to remove dental tartar without causing damage.

3.2.3. Microdosing

Microdosing is another application of piezoelectrics and has become popular because it conserves the amount of medication dispensed and can reduce discomfort by avoiding injections [99, 100]. In some cases, an injected drug can be aerosolized in order to avoid injection. In this case, piezoelectric vibrations can break the drug into fine particles which can be carried in an air stream and inhaled by the patient [100]. In the case of solids, a stacked actuator design is applicable by providing a single oscillation, rather than the consistent vibration of the previously mentioned ultrasonic devices. A glass tube is attached to the actuator and an electric signal stimulates the actuator providing a force to the tube and displacing a certain amount of the solid. Though the dispensing is very precise, it does have a minimum dosage and blockage can occur in the glass tube [101].

Stacked actuators in fluid pumps can administer small single doses or a continuous flow [102]. Fluid administration, like those for eye drops, often require small single doses [99]. A more complex form of controlled microdosing can be accomplished through a diaphragm pump [103]. This is more suited for some dosing systems such as insulin dispensing. One pump design places four chambers in series, with electrodes connecting the gate so they operate in tandem. Here the voltage controls the degree of membrane fluctuation and the phase of the material controls its direction [104]. An alternative design has parallel cylinders which are filled and emptied according to a certain sequence. The number of steps in the sequence determines the flow rate [105]. Though PZT is a popular material for biomedical pumps, polymer actuators such as PVDF-TrFE have been used as well [106].

3.2.4. Energy harvesting

In order to have implantable sensors within the body, they need to have a convenient source of energy. If the sensor is battery powered, future surgery will be required to extract and replace the battery. This is a current problem with pacemakers and limits the number of sensors placed after surgery. Energy harvesting through the body's movement via piezoelectricity is one way to avoid the need for battery incorporation or replacement. Energy harvesting from organs or the human body requires specific considerations, the most important being biocompatibility. Like implants, energy harvesting devices ideally should not contain hazardous chemicals, like lead, or must be sealable [107]. In the field of energy harvesting, one of the key modes of energy harvesting, a vibrating cantilever, is not as applicable to *in situ* biological energy

harvesting because a vibrating cantilever has a very high resonance frequency for peak power generation [108]. Though a cantilever's resonance frequency can be changed by altering its physical characteristics, such as adding a proof mass or increasing size [109], an implant needs to be small as to avoid interference with organ function [108]. Typically, piezoelectric biomedical harvesters will be thin films that target tiny irregular vibrations caused by normal organ deformation [110]. A piezoelectric energy harvester provides an AC power source, and the most energy is gained near the resonance frequency of the film [111]. This adds another engineering constraint as biological motions usually have low natural frequencies. The human heart beats at around 39 Hz and the frequency of someone walking is around 1 Hz [108, 112]. The energy harvesting element also has to be small, as large devices may impede the normal function of human organs or cause discomfort.

Most implanted devices should have some degree of flexibility for use in the human body. Both polymer and ceramic flexible devices can be adhered to consistently moving body parts to provide a source of energy. This could include wrapping a piezoelectric film around a pulsing artery or anchoring it to an expanding diaphragm, lung, or heart [108]. The heart, or locations near it, are advantageous places to put an energy harvesting device because they could power a pacemaker. Ceramic nanoribbons are usually attached to some flexible film such as polyimide, polyethylene terephthalate, or polyethylene naphthalate. The ceramic components, made of PMN-PT, PZT, or BaTiO$_3$, are fabricated in small units and then transferred to the flexible film [110]. PVDF and PVDF-TrFE thin films can also be used to fabricate energy harvesters. These films have the advantage of being biocompatible and do not have to be transferred onto a flexible matrix [113].

In replacement joints, stacked ceramic sheets are preferred for energy harvesting. Knee surgery is a difficult process and complications can arise after surgery [112]. The replacement joint can become imbalanced, and be subject to wear, loosening, or even fracture. The presence of sensors in the replacement joint vicinity would allow doctors to study how to improve knee replacements and detect problems with greater speed. The stacked actuator is the best design for energy harvesting in implanted joints. These actuators do not need to be as flexible, because the downward force from the knee is compressive, rather than stretching [114]. Prospective locations for the actuators could be in the tibial component of the joint or in the polyethylene cartilage imitation [112, 114].

The main limitations of piezoelectric energy harvesting are low efficiency and power output. This is large concern with biomedical devices, because they often do not operate at the device's resonance frequency [115]. Another avenue of research focuses on enhancing the efficiency of energy harvesting by mechanically scraping screening charges found on the surface of piezoelectric materials [116–119].

4. Conclusion

The purpose of this book chapter has been to give an overview of piezoelectric in the biomedical industry. We have described the piezoelectric properties of biological materials and how

they can be used to develop disease treatment. We also covered piezoelectric materials used in sensors, and other devices to explore the current industries which can be improved by further research. By describing these challenges, we hope to bring greater understanding of how important piezoelectricity is to the medical industry and the opportunities it has for future development.

Acknowledgements

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